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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
07/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/044,534	LE ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,7-10,14-16,18,19 and 21-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,7-10,14-16,18,19 and 21-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission, filed on 04/26/2007, has been entered.

Applicant's amendment, filed 04/26/2007, has been entered.

Claims 1, 3, 7 and 8 have been amended.

Claims 2, 4-6, 11-13, 17, 20 and 25-31 have been canceled previously

Claims 1, 3, 7-10, 14-16, 18-19 and 21-24 are pending.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

This Action will be in response to applicant's arguments, filed 04/26/2007.

The rejections of record can be found in the previous Office Action, mailed 10/23/2006.

3. Applicant's amended claims have obviated the previous rejection under 35 U.S.C. § 112, first paragraph, written description and under 35 U.S.C. § 112, second paragraph with respect to the recitation of "a pathology associated with increased TNFα concentrations relative to normal levels in the joints".

4. Priority.

The filing date of the instant claims which recite "a method of inhibiting TNFα in a human with increased TNFα concentrations relative to normal levels in the joints" is deemed to be the filing date of priority application USSN 08/192,861, filed 02/04/1994, now U.S. Patent No. 5,919,452.

Applicant's assertions concerning priority to the instant application or to priority USSN 07/943,852, filed 09/11/1992 of the newly added claimed limitation, drawn to "a method of inhibiting TNFα in a human with increased TNFα concentrations relative to normal levels in the joints" have been fully considered but are not found convincing.

Applicant's reliance upon various sections of the priority application USSN 07/943,852 to support the recitation of the newly amended claimed recitation of "a method of inhibiting TNFα in a human with increased TNFα concentrations relative to normal levels in the joints" is acknowledged.

However, the recitation of "a method of inhibiting TNFα in a human with increased TNFα concentrations relative to normal levels in the joints" is not readily apparent in the priority application USSN 07/943,852.

For example, while pages 40-41, overlapping paragraph of priority application USSN 07/943,852 describes "treating subject having a pathology or condition associated with excess of levels present in a normal healthy subject with anti-TNF antibodies";
This description on pages 40-41 of the priority document does not describe joints".

Further, this section appears limited to "rheumatoid arthritis" as a pathology or condition where "increased TNFα concentrations relative to normal levels in the joints" may be appropriate.

With respect to the other sections of with priority application USSN 07/943,852 that applicant relies upon for written support for the newly amended claims;
it appears that applicant relies upon a generic description of "treating subject having a pathology or condition associated with excess of levels present in a normal healthy subject with anti-TNF antibodies" and the presence of TNFα in rheumatoid arthritis joint tissues (e.g., see page 46, paragraph 1 of priority application USSN 07/943,852) and observations in the Examples in priority application USSN 07/943,852.

Also, it is noted that page 46, paragraph 1 of priority application USSN 07/943,852 discloses:
TNFα is of major importance in the pathogenesis of rheumatoid arthritis. TNFα is present in rheumatoid arthritis joint tissues and synovial fluid at the protein and mRNA level, indicating local synthesis. However, detecting TNFα in rheumatoid arthritis joints even in quantities sufficient for bioactivation does not necessarily indicate that it is important in the pathogenesis of rheumatoid arthritis, nor that it is a good candidate therapeutic target. In order to address these question, the effect of anti-TNF antibody on rheumatoid joint cell cultures, and for comparison, osteoarthritic cell cultures, have been studied. The initial result, that IL-1 production was abolished suggested that TNFα was a therapeutic target for the therapy of rheumatoid arthritis, since anti-TNFα antibodies would block both TNF and IL-1, the two cytokines known to be involved in cartilage and bone destruction.
Also, see Treatment of Arthritis, Sepsis, Allograft Rejection and Graft Versus Host Disease on pages 45-47 of priority application USSN 07/943,852

Therefore, the priority application USSN 07/943,852 appears to disclose that rheumatoid arthritis as the disease or condition targeted by anti-TNFα antibodies.

In addition, this priority document via the Detailed Description and Examples appears to describe joint inflammation as well as the role of TNFα in such joint inflammation in the context of rheumatoid arthritis and not as broadly as currently encompassed by the recitation of "treating subject having a pathology or condition associated with excess of levels present in a normal healthy subject with anti-TNF antibodies".

Also, as indicated above, the priority document USSN 07/943,852 appears to indicate that "detecting TNFα in rheumatoid arthritis joints even in quantities sufficient for bioactivation does not necessarily indicate that it is important in the pathogenesis of rheumatoid arthritis, nor that it is a good candidate therapeutic target"
which, in turn, appears in contrast to the current claimed recitation of "methods of inhibiting TNFα in a human with increased TNFα concentrations relative to normal levels of levels present in a normal healthy subject with anti-TNF antibodies".

In contrast to applicant's assertions that the priority application stands for broadly targeting patients with "increased TNFα concentrations in the joints with anti-TNFα antibodies"
a fair reading of the priority application USSN 07/943,852 would indicate that targeting patients with "increased TNFα concentrations relative to normal levels of levels present in a normal healthy subject with anti-TNF antibodies was not the intent of the priority document and that targeting a patient with joint inflammation with anti-TNFα antibodies would be based upon subsequent testing or investigation and on a case-by-case basis.

Further, the reliance upon the disclosure of the expression of TNF in joints and the monitoring of joint stiffness in rheumatoid arthritis patients in priority application USSN 07/943,852, does not support the broader recitation of "methods of inhibiting TNFα in a human with increased TNFα concentrations relative to normal levels of levels present in a normal healthy subject with anti-TNF antibodies", as currently claimed.

The instant claims now recite limitations which were not clearly disclosed in the priority applications as well as the specification as-filed, and would have changed the scope of the priority application as-filed.

It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

Also, it is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977).

Also, applicant is reminded that a species reads on a genus.

Therefore, prior art referenced methods of treating "rheumatoid arthritis" anticipates the more generic recitation of "methods of inhibiting TNFα in a human with increased TNFα concentrations relative to normal levels in the joints", as currently claimed.

Applicant's assertions concerning priority of the instant claims have not been found persuasive.

If applicant desires priority prior to the instant application, applicant is invited to point out and provide documentary support for the priority of the instant claims.

Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention.

6. Claims 1, 3, 7-10, 14-16, 18-19 and 21-24 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3, 7-10, 14-16, 18-19 and 21-24 are indefinite in the recitation of "a method of inhibiting TNFα in a human with increased TNFα concentrations relative to normal levels in the joints" because the metes and bounds of said "increased TNFα concentrations relative to normal levels in the joints" are ill-defined and unclear. The recitation of "increased TNFα concentrations relative to normal levels in the joints" is relative in nature which renders the claims indefinite. These relative phrases of "increased concentrations" and "normal levels" are not defined by the claims and the specification does not provide a standard for ascertaining the requisite degree and, in turn, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Also, as noted above in the Section on Priority, page 46, paragraph 1 of priority application USSN 07/943,852 discloses:
TNFα is of major importance in the pathogenesis of rheumatoid arthritis. TNFα is present in rheumatoid arthritis joint tissues and synovial fluid at the protein and mRNA level, indicating local synthesis. However, detecting TNFα in rheumatoid arthritis joints even in quantities sufficient for bioactivation does not necessarily indicate that it is important in the pathogenesis of rheumatoid arthritis, nor that it is a good candidate therapeutic target. In order to address these question, the effect of anti-TNF antibody on rheumatoid joint cell cultures, and for comparison, osteoarthritic cell cultures, have been studied. The initial result, that IL-1 production was abolished suggested that TNFα

was a therapeutic target for the therapy of rheumatoid arthritis, since anti-TNFα antibodies would block both TNF and IL-1, the two cytokines known to be involved in cartilage and bone destruction.

Also, see Treatment of Arthritis, Sepsis, Allograft Rejection and Graft Versus Host Disease on pages 45-47 of priority application USSN 07/943,852

As indicated above, the priority document USSN 07/943,852 appears to indicate that "detecting TNFα in rheumatoid arthritis joints even in quantities sufficient for bioactivation does not necessarily indicate that it is important in the pathogenesis of rheumatoid arthritis, nor that it is a good candidate therapeutic target"

which, in turn, appears in contrast to the current claimed recitation of "methods of inhibiting TNFα in a human with increased TNFα concentrations relative to normal levels of levels present in a normal healthy subject with anti-TNF antibodies".

There is insufficient description of the nature and targeted "pathologies associated with increased TNFα concentrations relative to normal levels in the joints" to apprise the ordinary artisan of the metes and bounds of the claimed methods.

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06.

7. As indicated above in the Section on Priority,

the filing date of the instant claims which recite "a method of inhibiting TNFα in a human with increased TNFα concentrations relative to normal levels in the joints" is deemed to be the filing date of priority application USSN 08/192,861, filed 02/04/1994, now U.S. Patent No. 5,919,452.

Applicant's amendment and arguments, filed 04/26/2007, have been fully considered but are not found convincing essentially for the reasons set forth above with respect to priority back to priority application USSN 07/943,852.

Claims 1, 3, 7-10, 14-16, 18-19 and 21-24 are rejected under 35 U.S.C. § 102(b) as being anticipated by Le et al. (WO 92/16553) (1449; #AN4) (see entire document, including Claims 40-41).

Le et al. teach methods of treating TNF-related pathologies, including rheumatoid arthritis (e.g., see page 8, paragraph 3; page 34, paragraph 1; Claims 40-41) with TNF-α-specific antibodies, including recombinant and chimeric antibodies and the cA2 antibody specificity of the instant invention by administering the recombinant A2 or cA2 antibody and fragments thereof (e.g. see pages 9-11; page 13, paragraph 1 and Examples on pages 45- 74) (see entire document, including Summary of the Invention, Detailed Description of the Preferred Embodiments, and Claims).

Also see pages 34-38 for the well known dosing and modalities of administering therapeutic antibodies of interest to meet the needs of the patients as well as the Examples for affinity constants of prior art cA2-specific antibodies.

Given the teaching of antibodies that bind the same epitope that are recognized by the cA2 anti-TNF antibody as well as the A2 and cA2 antibodies themselves, the prior art teaches antibodies that bind the identical epitope of the A2 and cA2 antibodies. Given the prior art teachings drawn to the same chimeric A2 and cA2 antibodies and/or the same A2 and cA2 starting materials, the specific antibody regions comprising SEQ ID NOS: 2, 3,4 and/or 5 as well as binding a neutralizing epitope of human would be inherent properties of the prior art recombinant A2 and cA2 antibodies.

It appears that the prior art methods do not result in a manipulative difference between the prior art and the claimed methods.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods to treat rheumatoid arthritis with recombinant cA2-specific antibodies.

A species anticipates a claim to a genus. See MPEP 2131.02.

Applicant's arguments based upon priority have not been found persuasive.

8. Again, it is noted that applicant has a number of copending applications in the instant family of applications with the same A2 / cA2 TNF-specific antibodies.

Again, given the history of a number of continuations-in-part, it is not readily apparent whether the claims were subject to restriction and whether the claims are subject to double patenting rejections.

Applicant is invited to clarify which applications should be subject to rejections under the judicially created doctrine of obviousness-type double patenting.

9. Claims 1, 3, 7-10, 14-16, 18-19 and 21-24 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over
claims 1-16 of U.S. Patent No. 5,698,195 (1449; #AD3);
claims 1-13 of U.S. Patent No. 5,919,452 (892; of record);
claims 1-34 of U.S. Patent No. 7,179,466 (1449; #AB4);
claims 1-30 of U.S. Patent No. 7,166,284 (1449; #AD4); and
claims 1-26 of U.S. Patent No. 7,138,118 (1449; #AG4).

Although the recitation of the instant and patented claims differ, all of the instant and patented claims are drawn to the same or nearly the same A2/cA2-specific TNF-α-specific antibodies having the same or nearly the same functional properties of neutralizing TNF-α in the treatment of TNF-related conditions, such as rheumatoid arthritis as well as other inflammatory /autoimmune conditions. The patented claims anticipate or render obvious the instant "methods of inhibiting TNFα in a human with increased TNFα concentrations relative to normal levels in the joints"

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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